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| EXAMINER | |
|---|---|
| BLUMEL, BENJAMIN P | |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/666,833 | SEGAL ET AL. | |
| | Examiner | Art Unit | |
| | BENJAMIN P. BLUMEL | 1648 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *05 August 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *4* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 5-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/24/2010 and 8/5/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Applicants are informed that Examiner Blumel will be examining the instant application.

Applicants are informed that the rejections of the previous Office action not stated below have been withdrawn from consideration in view of the Applicant's arguments and/or amendments.

### Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/5/2010 has been entered.

Claims 1-3 and 5-13 are examined on the merits. Claim 4 remains withdrawn as it is drawn to a non-elected species.

### Information Disclosure Statement

The information disclosure statements (IDSs) submitted on 2/24/2010 and 8/5/2010 were filed after the mailing date of the final Office action on 12/10/2009. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

### Response to Arguments

Applicant's arguments filed 8/5/2010 have been fully considered but they are not persuasive. See responses below.

## Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

**(New Rejection)** Claims 1-3 and 5-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites, "…fusion polypeptide bound to a carbohydrate on said antigen bearing target and includes said polypeptide which is not bound to said antigen bearing target…", however, since claim 1 recites multiple polypeptides (see lines 2, 3, 7 and 8), it is unclear which polypeptide the limitation of not being bound to the antigen bearing target is referring to. Claims 2, 3 and 5-13 are rejected since they depend from claim 1.

Claim 3 recites the limitation "vaccine" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 8 recites, "…target is a cell which is substantially unable to divide.", however, it is unclear what the metes and bounds of "substantially" are.

## Double Patenting

In response to the double patenting rejections set forth in the previous office action, and restated below, Applicant submits that upon notification of otherwise allowable subject matter in the instant case, Applicants will address the double patenting rejections.

Applicant's intention is noted. However, until the rejections are properly addressed, with the submission of a terminal disclaimer, all double patenting rejections are maintained for the reason(s) set forth in the record.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Omum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

**(Prior Rejection Re-instated)** Claims 1-3 and 5-13 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 and 5-11 of copending Application No. 10/666,886. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant invention and the invention of the co-pending application are drawn to variations of a

composition which contains an antigen bearing target, such as a mammalian cell and a fusion polypeptide that contains either an amino acid sequence that binds to a carbohydrate or a sequence that comprises a cell-surface binding moiety fused to a ligand for a GM-CSF receptor on the surface of a leukocyte. As a result, the claimed invention of '886 renders the instant invention obvious.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

**(Prior Rejection Re-instated)** Claims 1-3 and 5-13 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 4-14 of U.S. Patent No. 7,629,440 (US Patent Application 10/224,661). Although the conflicting claims are not identical, they are not patentably distinct from each other because while the patented invention is drawn to a fusion polypeptide with a first amino acid sequence containing an influenza virus Hemagglutinin protein (a protein that binds to a sialic acid on the surface of a cell) and a second amino acid sequence of a GM-CSF molecule that can bind to its receptor, the disclosure of '440 also teaches a method of using a composition containing such a fusion protein linked to an antigen bearing target, such as a mammalian cell that can not divide, more specifically a leukocyte or antigen presenting cell in a composition. This same composition can also contain the fusion protein not linked to the antigen bearing target. (See Columns 9 and 10). This rejection is necessitated by the decision of the Court of Appeals for the Federal Circuit in Pfizer Inc. v Teva pharmaceuticals USA Inc., 86 USPQ2d 1001, at page 1008 (March 2008), which indicates that there is no patentable distinction between claims to a product and a method

of using that product disclosed in the specification of the application and that the preclusion of such a double patenting rejection under 35 USC 121 does not apply where the present application is other than a divisional application of the patent application containing such patentably indistinct claims.

Therefore, since the patented invention and the teachings of its disclosure produce the claimed composition, the instant invention is obvious to one of ordinary skill in the art.

**Response to arguments:**

Applicants state that upon notification of otherwise allowable subject matter in the instant case, they will timely file a terminal disclaimer to obviate the double patenting rejection.

## Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

**(New Rejection)** Claims 1-3 and 5-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hoo (US Pat. 5,891,432) and Scholler et al. (Journal of Immunology, 2001).

The claims are directed to a composition comprising a mammalian cell (antigen bearing target), and a fusion polypeptide comprising i) a first amino acid sequence that can bind a carbohydrate and ii) a second amino acid sequence comprising a ligand for a cell surface polypeptide of a leukocyte. The composition also includes the cell and the fusion polypeptide

being bound via a carbohydrate on said cell and a polypeptide not bound to the cell. Claim 2, which depends on claim 1, limits the second amino acid sequence to a ligand for a cytokine receptor, which is limited to GM-CSF by claim 3. Claim 5, which depends on claim 1, requires the cell to be a mammalian cell. Claim 6, which depends on claim 5, requires the cell to be a pathogenic cell. Claim 7, which depends on claim 5, requires the cell to be an attenuated cell. Claim 8, which depends on claim 1, requires the cell to be unable to divide. Claim 9, which depends on claim 1, requires the leukocyte to be an antigen presenting cell, which is specified as a professional antigen presenting cell by claim 10 and dendritic cell by claim 11. In addition, the first amino acid sequence can bind to a sialic acid on a glycoprotein or a carbohydrate-binding domain of a naturally occurring lectin.

The Prior Art

Hoo teaches a composition comprising a cell (antigen bearing target) and a fusion polypeptide containing a membrane attachment domain and cytokine which is a ligand for a cytokine receptor. Hoo also teaches that the composition can contain the fusion protein attached to the cell and a soluble secondary immunomodulatory molecule, such as a cytokine (i.e., protein) in a membrane bound form or in a soluble form (see column 18, lines 33-62). The antigen bearing target that Hoo teaches includes a virus, a bacterial cell, fungal cell, a cell of a parasite, a mammalian cell, pathogenic and attenuated antigens, and a cell that is substantially unable to divide. [Lines 35-45, column 10, and columns 9-18, in particular.]

The first amino acid sequence in the fusion polypeptide of Hoo comprises the sequence to a membrane attachment domain, a cell-surface binding moiety, such as a domain that spans the width of a cell membrane or any part thereof. More specifically, CD molecules, or a

phosphatidylinositol-glycan anchor that binds to the CT domain of a cell membrane protein can be used as a membrane attachment domain. (See columns 7-8). The second amino acid sequence in the fusion polypeptide of Hoo comprises the sequence of a ligand for a cell surface polypeptide of a leukocyte. Specifically, the ligand for a cell surface polypeptide of a leukocyte is a ligand for a cytokine receptor. In particular, the ligand for a cytokine receptor that Hoo et al. teaches is GM-CSF. [Example I, column 22, in particular.] The ligand for a cell surface polypeptide used by Hoo is a ligand for a cell surface polypeptide of a leukocyte, wherein the leukocyte is dendritic cells, which is a professional antigen presenting cell. [Columns 1-2, in particular.] In the instant case, the composition of Hoo is the same as the claimed invention.

However, Hoo does not specifically teach the binding of the fusion polypeptide via a carbohydrate on a cell through a first amino acid sequence that can bind to sialic acids on a glycoprotein or a sequence that comprises a carbohydrate binding domain of a naturally lectin.

Scholler et al. teach the binding of a fusion protein to sialic acids on a glycoprotein on the surface of a cell. More specifically, Scholler et al. teach that a CD83 molecule fused to a mutated Ig constant region can selectively bind to some CD8+ T cells and Monocytes via sialic acids of a carbohydrate epitope. As a result, CD83 can be considered a sialic acid binding lectin. Therefore, CD83 is a naturally occuring lectin since it can be found on mature dendritic cells. See page 3865.

It would have been obvious to one of ordinary skill in the art to modify the composition taught by Hoo in order to use generate a composition containing a fusion protein bound via a carbohydrate to a cell and a non-bound polypeptide, wherein the fusion protein contains an amino acid sequence that can bind to sialic acid on a glycoprotein and contains a carbohydrate

binding domain of a naturally occurring lectin. One would have been motivated to do so, given the suggestion by Hoo that the cell-binding moieties be use to associate a fusion polypeptide with a membrane of a cell, such as using CD antigens as the attachment factor. There would have been a reasonable expectation of success, given the knowledge that CD83 fused to another protein fragment can bind to sialic acids on a glycoprotein and therefore contains a carbohydrate binding domain of a naturally occurring lectin, as taught by Scholler et al. Thus the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

**Response to arguments:**

Applicants argue that Hoo does not teach the binding of the fusion protein to the antigen bearing target via a carbohydrate on the antigen bearing target and that the fusion protein of Hoo does not contain a carbohydrate binding domain. In addition, Hoo does not teach that the fusion protein can be in bound and unbound forms in the composition.

It is acknowledged that Hoo does not specifically state that a carbohydrate on the antigen bearing target is used to bind the fusion protein. However, Hoo does teach that the composition can contain both cell-bound fusion protein and either an additional bound fusion protein of an immunomodulatory molecule (i.e., cytokine) or a soluble version of the molecule (see above. Furthermore, since Scholler et al. teach the binding of sialic acids on a carbohydrate epitope by their CD83 fusion protein, and since Hoo teaches that CD antigens can be used as a membrane attachment molecules in the fusion protein the instant invention is prima facie obvious to one of ordinary skill in the art at the time the invention was made.

## Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BENJAMIN P. BLUMEL whose telephone number is (571)272-4960. The examiner can normally be reached on M-F, 8-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Zachariah Lucas can be reached on 571-272-0905. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/BENJAMIN P BLUMEL/
Examiner
Art Unit 1648